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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,987	DREHER ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-48* is/are pending in the application.

4a) Of the above claim(s) *42-45 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-41,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/05,4/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 39-41, 46-47) and the species election of SEQ ID NO: 4 in the reply filed on 17 October 2006 is acknowledged.

2. Claims 42-45 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 October 2006.

Formal Matters

3. Claims 39-48 are pending. Claims 42-45 and 48 are withdrawn from consideration as being drawn to non-elected inventions. Claims 39-41 and 46-47 are under examination as they read on the elected species of SEQ ID NO: 4.

Information Disclosure Statement

4. The information disclosure statements filed on 6 May 2005 and 27 April 2006 have been considered to the fullest extent possible. Signed copies are attached hereto. Both IDS documents contain references that are not in the English language. These documents have been lined through on the PTO-1449 forms. The Examiner will be happy to consider these documents if and when an English translation is provided.

Specification - Objection

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: IL-15 IgG fusion protein.

6. The use of numerous trademarks have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. For example, see, CLONTECH (p. 11), PROMEGA (p. 11), STRATAGENE (pp. 11, 41, 43), INVITROGEN (pp. 11, 40), AMERSHAM PHARMACIA (pp. 41, 46), QIAGEN (pp. 41, 44, 45), DULBECCO'S (p. 45), BIOWHITTAKER (p. 45), BD BIOSCIENCES (pp. 46, 47), PHARMINGEN (pp. 46-47), NALEGENE-NUNC (p. 46), PIERCE (p. 46), BECTON-DICKINSON (p. 46), R&D SYSTEMS (p. 47), ROCHE (p. 48).

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claims 39-41 are objected to because of the following informalities: claim 39 recites "[a] fusion protein composed of..." The term "composed of" is non-standard language. It is unclear whether Applicant means "comprising" or "consisting of". Similarly, claim 41 uses the term "contains" in line 1 of the claim. In order to expedite prosecution, the claims will be read as using the tem "comprising" in place of the terms "composed of" and "contains". Appropriate correction is required.

8. Claim 46 is objected to because of the following informalities: the claim is missing an initial article. It is unclear whether the applicant is referring to "a" method or "the" method. For purposes of expediting prosecution, the claim will be read as "a" method. Appropriate correction is required.

9. Claim 47 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. Claim 47 refers to claim 39 in the preamble including a step of introducing at least one nucleic acid as claimed in claim 42. See MPEP § 608.01(n). Claim 47 is also objected to for depending from a withdrawn claim. Because the nucleic acids of claim 42 are withdrawn from consideration, by Applicant's election, the nucleic acids of claim 42 will not be considered in the examination of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

Enablement

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim recites [a] method of preventing and/or treating

transplantation sequelae and/or autoimmune diseases, wherein a fusion protein as claimed in claim 398 or a nucleic acid as claimed in claim 42 is administered to a subject.

The specification does not reasonably provide enablement for prophylaxis (prevention) of organ transplantation sequelae and/or autoimmune diseases in any species by any means. The skilled artisan cannot envision the prevention of organ transplantation sequelae and/or autoimmune diseases. Prevention involves "attacking" the underlying cause of organ transplantation sequelae and/or autoimmune diseases; i.e., disrupting the mechanisms which give rise to organ transplantation sequelae and/or autoimmune disease. The skilled artisan is aware that the causes of all organ transplantation sequelae and/or autoimmune diseases were unknown at the time of the invention herein. For purposes of enablement, the specification must provide reasonable detail in order for those skilled in the art to carry out the invention. In this case, the specification must disclose a means of preventing organ transplantation sequelae and/or autoimmune diseases regardless of the underlying causes of the organ transplantation sequelae and/or autoimmune diseases. The teachings of the specification do not enabled a person of ordinary kill in the art to make and use the claimed method of prophylaxis. Moreover, "[p]atent protection is granted only in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d at 1366, 42 USPQ2d at 1005 (Fed. Cir.), cert. denied, 118 S. Ct. 397 (1997), ("Tossing out the mere germ of an idea does not constitute an enabling disclosure").

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 39-41, 46, and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the fusion protein comprising SEQ ID NO: 4, does not reasonably provide enablement for a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims recite a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment; characterized in that the IgG Fc fragment is a human or murine IgG1, a human IgG2, a murine IgG2a, a human or murine IgG3 or a human IgG4; which [comprises] an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5 or an allelic variant thereof; [A] method of preventing and/or treating transplantation sequelae and/or autoimmune diseases, wherein a fusion protein as claimed in claim 398 or a nucleic acid as claimed in claim 42 is administered to a subject; a process for preparing a fusion protein as claimed in claim 39 comprising the following steps (a) introducing at least one nucleic acid as claimed in claim 42 and/or at least one vector containing at least one nucleic acid as claimed in claim 42 into a cell and (b) expressing the nucleic acid under suitable conditions.

The nature of the invention is drawn to a wild-type IL-15 IgG fusion protein. The state of the art discloses genetically constructed and expressed mutant IL-15/IgGFcγ2a fusion protein mutants (Kim et al., J Immunol. 1998 Jun 15;160(12):5742-8; p. 5743, column 1). The process for producing the fusion protein in a vector and expressing the vector under suitable conditions is described by Kim et al., at p. 5743, column 1. Kim et al., also teach that the IL-15 mutant/Fcγ2a fusion protein markedly attenuated antigen-specific delayed-type hypersensitivity responses and decreased leukocyte infiltration within the delayed-type hypersensitivity sites (abstract). Kim et al., also teach a method of treating autoimmune disease and organ transplantation with IL-15 mutant/Fc γ2a protein (p. 5747, column 1, last two paragraphs). Kim et al., do not teach a fusion protein comprising wild-type IL-15.

The level of skill of those in the art is high in light of genetic recombination techniques needed to produce fusion proteins. However, the construction and expression of fusion proteins in vectors is well known and is routine in the art.

There is one working model of a wtIL-15/IgG Fc protein disclosed in Example 5 of the specification (pp. 44-45). Although working examples are not required, they tend to provide additional evidence of how to make and/or use a claimed invention. However, in this case, the description of the wild-type IL-15 fusion protein is limited to the name of the fusion protein only. No structural information

is provided in the example. It is noted that the murine mutant IL-15/IgG Fc protein is better described than the wild-type IL-15 fusion protein in the Example.

The claims are drawn to a fusion protein comprising wild-type IL-15 (wtIL-15) and an IgG Fc fragment. However, the specification fails to provide sufficient guidance such that the species from which the wtIL-15 and IgG Fc fragment may be determined. For example, in claims 39 and 40, it is unclear whether the 162 amino acid sequence from the human or murine wtIL-15 is intended or the 128 amino acid protein of canis familiaris. Additionally, there is insufficient guidance to determine whether the entire wtIL-15 protein is to be used in the fusion protein, or merely the 114 amino acid active protein is to be included, or some portion thereof. Further, there is insufficient guidance in the disclosure to determine which Fc fragment is to be used in the fusion protein of claim 39 and from which IgG subtype (i.e. IgG1, IgG2, IgG3, IgG4) of which species (human, murine, etc.) the Fc fragment is to be derived. Further, no guidance is given such that the person of ordinary skill in the art would understand which portion of an IgG Fc fragment is intended by Applicant's claims. Without the requisite IL-15 or IgG Fc structural information, such as the metes and bounds of the amino acid sequences to be included or excluded (i.e. the entire 162 amino acid human wild-type IL-15 protein or just the 128 amino acid functional protein), creation of the wtIL-15/IgG-Fc fusion protein, as presently claimed, would require undue experimentation.

Claim 41 recites an allelic variant of SEQ ID NOs: 1, 2, 3, 4, and 5. However, no guidance is provided such that one of ordinary skill in the art may determine which proteins constitute an allelic variant. Claim 41 is drawn to a fusion protein, which is an artificial construct. It is unclear whether the claimed allelic variant is meant to be an allelic variant of the wtIL-15 portion of the fusion protein or an allelic variant of the claimed IgG Fc fragment portion of the fusion protein.

Therefore, based on the discussions above concerning the art's recognition that IL-15/IgG-Fc fusion proteins are known in the art, but neither the instant claims nor the disclosure recite the metes and bounds of the claimed wtIL-15/IgG-Fc protein, such that a person of ordinary skill would be able to make or use the claimed protein, the specification fails to teach the skilled artisan how to use the claimed methods without resorting to undue experimentation to determine which amino acids of the wtIL-15 protein are to be included in the fusion protein and which IgG Fc fragments are to be used.

Due to the large quantity of experimentation necessary to determine which amino acids of the wtIL-15 protein are to be included in the fusion protein and which IgG Fc fragments are to be used, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art

establishing that other IL-15/IgGFc fusion proteins are known, and the breadth of the claims which fail to recite specific structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 46 and 47 are rejected insofar as they depend on and/or are dependently linked to rejected claims.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

14. Claims 39-41, 46, and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims recite a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment; characterized in that the IgG Fc fragment is a human or murine IgG1, a human IgG2, a murine IgG2a, a human or murine IgG3 or a human IgG4; which [comprises] an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5 or an allelic variant thereof; [A] method of preventing and/or treating transplantation sequelae and/or autoimmune diseases, wherein a fusion protein as claimed in claim 398 or a nucleic acid as claimed in claim 42 is administered to a subject; a process for preparing a fusion protein as claimed in claim 39 comprising the following steps (a) introducing at least one nucleic acid as claimed in claim 42 and/or at least one vector containing at least one nucleic acid as claimed in claim 42 into a cell and (b) expressing the nucleic acid under suitable conditions.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics; structure/function correlation. methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* SEQ ID NO: 4, as elected. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 46 and 47 are rejected insofar as they depend on and/or are dependently linked to rejected claims.

Claim Rejections - 35 USC § 112, Second Paragraph

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "organ transplantation sequelae" and/or autoimmune diseases. The metes and bounds of "organ transplantation sequelae" are not disclosed in the specification such that one would know which sequelae Applicant's intended. Additionally, it is unclear which autoimmune diseases are intended to be treated and/or prevented. The metes and bounds of number and types of autoimmune diseases is not limited.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 39-40, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al., J Immunol. 1998 Jun 15;160(12):5742-8.

The claims recite a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment; characterized in that the IgG Fc fragment is a human or murine IgG1, a human IgG2, a murine IgG2a, a human or murine IgG3 or a human IgG4; [A] method of preventing and/or treating transplantation sequelae and/or autoimmune diseases, wherein a fusion protein as claimed in claim 398 or a nucleic acid as claimed in claim 42 is administered to a subject; a process for preparing a fusion protein as claimed in claim 39 comprising the following steps (a) introducing at least one nucleic acid as claimed in claim 42 and/or at least one vector containing at least one nucleic acid as claimed in claim 42 into a cell and (b) expressing the nucleic acid under suitable conditions.

Kim et al., teach a genetically constructed and expressed a receptor site-specific IL-15 antagonist IgG fusion protein mutant with by mutating glutamine residues within the C terminus of IL-15 to aspartic acid and genetically linked this mutant IL-15 to murine Fc gamma2a (p. 5743, column 1). The process for producing the fusion protein in a vector and expressing the vector under suitable conditions is described at p. 5743, column 1. Kim et al., also teach that the IL-15 mutant/Fc gamma2a fusion protein markedly attenuated antigen-specific delayed-type hypersensitivity responses and decreased leukocyte infiltration within the delayed-type hypersensitivity sites (abstract). Kim et al., also teach a method of treating autoimmune disease and organ transplantation with IL-15 mutant/Fc gamma2a protein (p. 5747, column 1, last two paragraphs). Kim et al., do not teach a fusion protein comprising wild-type IL-15.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have constructed a wild-type IL-15/Ig-Fcγ2a fusion protein. Kim et al., state that they constructed their IL-15 mutant/Ig-Fcγ2a fusion protein because the half-life of the unmodified wild-type IL-15 protein is short (see p. 5744, column 1, second paragraph) and they wanted a fusion protein with a longer half-life, which would be of greater therapeutic benefit. A person reasonably would have expected success in creating a wild-type IL-15/IgG fusion protein because Kim et al., were successful in creating a mutant IL-15/IgG fusion protein, the mutant comprising mutating glutamine residues within the C-terminus of IL-15 to aspartic acid. The points of substitution mutation had previously been shown not to interfere with IL-15 binding or function (see p. 5744, column 1, second paragraph). Additionally, it would have been obvious to use the wild-type IL-15/IgG Fc fusion protein in the treatment of organ transplantation sequelae or autoimmune disease because of the teachings of Kim et al.

21. Claims 39-40, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strom al., US Patent 6,001,973 (14 December 1999).

The claims recite a fusion protein [comprising] a wild-type IL-15 and an IgG Fc fragment with the exception of a murine IgG2b Fc fragment; characterized in that the IgG Fc fragment is a human or murine IgG1, a human IgG2, a murine IgG2a, a human or murine IgG3 or a human IgG4; [A] method of preventing and/or treating transplantation sequelae and/or autoimmune diseases, wherein a fusion protein as claimed in claim 398 or a nucleic acid as claimed in claim 42 is administered to a subject; a process for preparing a fusion protein as claimed in claim 39 comprising the following steps (a) introducing at least one nucleic acid as claimed in claim 42 and/or at least one vector containing at least one nucleic acid as claimed in claim 42 into a cell and (b) expressing the nucleic acid under suitable conditions.

Strom et al., teach a human IL-15/IgG-Fc fusion protein bearing a double mutation Q149D; Q156D) designed to target the putative sites critical for binding to the IL-2Rγ subunit. The polar, but uncharged glutamine residues at positions 149 and 156 were mutated into acidic residues of aspartic acid utilizing PCR-assisted mutagenesis, in order for the fusion protein to act as an antagonist to wild-type IL-15 (column 23, lines 42-48). Methods of treating autoimmune diseases are taught at columns 9 and 10 and methods of treating organ transplantation sequelae are taught at column 8. Construct of the fusion protein using an expression vector are taught at column 15.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have constructed a wild-type IL-15/Ig-Fcγ2a fusion protein. Strom et al., state that they constructed their IL-15 mutant/Ig-Fc fusion protein because they wanted to antagonize endogenous IL-15 binding. A person reasonably would have expected success in creating a wild-type IL-15/IgG fusion protein because Strom et al., were successful in creating a mutant IL-15/IgG fusion protein using PCR-assisted mutagenesis. Additionally, it would have been obvious to use the wild-type IL-15/IgG Fc fusion protein in the treatment of organ transplantation sequelae or autoimmune disease because of the teachings of Strom et al.

Conclusion

22. It is noted that the amino acid sequence of SEQ ID NO: 4 is free of the prior art.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CMW

AU 1647

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER